Palladium-Catalyzed Carbonylative Cross-Coupling Reaction with Triethyl(1-methylindol-2-yl)borate: A Simple Route to 1-Methylindol-2-yl Ketones

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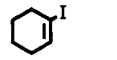
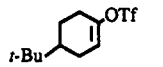
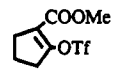
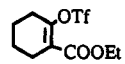
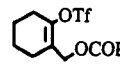
The carbonylative cross-coupling reaction has recently arisen as a useful synthetic tool for ketone synthesis, where various kinds of organometallic compounds have been used for these transformations.[1] Recent reports have proven alkenyltin and trivalent boron compounds to be promising substrates, because of their ready availability and vast spectrum of applicability.[2] However, employment of tetravalentboron compounds in this process is known to be problematic.[3]

In our studies designed to further probe the synthetic utility of indolylborate intermediate,[4] we have previously reported a successful palladium-catalyzed cross-coupling reaction of triethyl(1-methylindol-2-yl)borate (**1a**), which is a tetravalent boron compound.[5] Our subsequent attention was drawn to the question as to whether borate **1a** might be applicable to the carbonylative cross-coupling reaction as well.

Generally, indolyl ketones could be prepared by treating zinc and magnesium salts of indoles with acid chlorides or by Hoesch Friedel–Craft synthesis, processes which are generally amenable to the synthesis of indol-3-yl ketones with limited application to the synthesis of indol-2-yl ketones.[6]

Here, we report that borate **1a**, generated *in situ* from 2-lithio-1-methylindole and triethylborane, undergoes a palladium-catalyzed carbonylative cross-coupling reaction to form indol-2-yl ketones **3**.

Table 1. Preparation of 1-Methylindol-2-yl Ketones 3

R-X (2)	condns[a] (solvent/temp (°C)/time (h))	yield[c] (%) 3	4	5
C_6H_5Br	xylene/90/60	20 (**3a**)	10 (**4a**)	50
C_6H_5I	THF/reflux/20[b]	36 (**3a**)	20 (**4a**)	22
C_6H_5I	THF/60/20	55 (**3a**)		28
C_6H_5I	xylene/90/60	80 (**3a**)		3
o-MeC_6H_4I	xylene/90/ 60	73 (**3b**)		10
p-MeC_6H_4I	xylene/90/6 0	76 (**3c**)		5
p-BrC_6H_4I	xylene/90/60	72 (**3d**)		10
p-$MeOOCC_6H_4I$	xylene/90/60	20 (**3e**)	20 (**4b**)	5
p-$MeCOC_6H_4I$	xylene/90/40	*d*		
(*E*)-$C_6H_5CH{=}CHBr$	xylene/90/20	28 (**3f**)		10
(*E*)-$C_6H_5CH{=}CHI$	THF/60/20	78 (**3f**)		2
	THF/60/40	65 (**3g**)		5
	THF/rt/10 days	80 (**3h**)		3
	THF/60/40	77 (**3h**)		10
	THF/60/40	46 (**3i**)	27 (**4c**)	5
	THF/60/40	64 (**3j**)	3 (**4d**)	5
	THF/60/40	60 (**3k**)	9 (**4e**)	5

[a] Carbon monoxide (15 atm). [b] Carbon monoxide (1 atm). [c] Isolated yields based on 1-methylindole. [d] No isolable product.

The palladium-catalyzed carbonylative cross-coupling reaction of borate **1a** proceeded readily under carbon monoxide (15 atm) at 60 °C in THF with vinyltriflates, whereas slightly forcing conditions were required for iodobenzene derivatives. Table 1 summarizes the results of this simple transformation of borate **1a** to indol-2-yl ketones **3**. The stated yields represent the two-step sequence of converting 1-methylindole into indol-2-yl ketone **3**.

The attempted reaction of borate **1a** with bromobenzene and β-bromostyrene was quite sluggish, and efforts to influence the reaction by varying temperature, solvent, and Pd catalyst did not lead to improvement. With both iodides and vinyl triflates, the carbonylation of borate **1a** proceeded in good yields except for iodobenzene having an electron-withdrawing group (4-COOMe, 4-COMe) in the aromatic ring.[7] The carbonylation reaction of borates **1b** and **1c** with iodobenzene under the same conditions was markedly retarded: 42% yield of ketone **6** from **1b** and only a trace amount of ketone **7** from **1c**. Adding Pd catalyst to a solution of borate **1a** and R-X **2** (2-carbomethoxycyclopenten-1-yl triflate) at room temperature under carbon monoxide atmosphere led to the sole formation of **4c** (70% yield). However, preferential formation of ketone **3i** was attained by the addition of Pd catalyst under cooling.

These results could be rationalized in terms of a common reaction path in Scheme 2.[2c,8] (1) Cross-coupling reaction

(1) (a) Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5546. (b) Izumi, T.; Iino, T.; Kasahara, A. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 2251. (c) Larock, R. C.; Hershberger, S. S. *J. Org. Chem.* **1980**, *45*, 3840. (d) Kobayashi, T.; Tanaka, M. *J. Organomet. Chem.* **1981**, *205*, C27. Tanaka, M. *Synthesis* **1981**, 47. Tamaru, Y; Ochiai, H.; Yamada, Y.; Yoshida, Z. *Tetrahedron Lett.* **1983**, *24*, 3869. (e) Bumajin, N. A.; Ponomaryov, A. B.; Beletskaya, I. P. *Tetrahedron Lett.* **1985**, *26*, 4819. (f) Wakiya, Y.; Yasunaga, T.; Kojima, M. *J. Organomet. Chem.* **1985**, *288*, 261. (g) Heck, R. F. *Palladium Reagents in Organic Syntheses*; Academic Press Inc.: London, 1985. (h) Kobayashi, T.; Tanaka, M. *Tetrahedron Lett.* **1986**, *27*, 4745. (i) Kikukawa, K.; Idemoto, T.; Katayama, A.; Kuno, K.; Matsuda, T. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1511. (j) Yamashita, H.; Kobayashi, T.; Sakakura, T.; Tanaka, M. *J. Organomet. Chem.* **1988**, *356*, 125. (k) Hatanaka, Y.; Hiyama, T. *Chem. Lett.* **1989**, 2049. Hatanaka, Y.; Fukushima, S.; Hiyama, T. *Tetrahedron* **1992**, *48*, 2113.

(2) (a) Grisp, G. T.; Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 7500. (b) Goure, W. F.; Wright, M. F.; Davis, P. D.; Labadie, S. S.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 6417. (c) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. (d) Wakita, Y.; Yasunaga, T.; Akita, M.; Kojima, M. *J. Organomet. Chem.* **1986**, *301*, C17. Kondo, T.; Tsuji, Y.; Watanabe, Y. *J. Organomet. Chem.* **1988**, *345*, 387; (e) Kwon, H. B.; Mckee, B. H.; Stille, J. K. *J. Org. Chem.* **1990**, *55*, 3114. (f) Gyorkos, A. C.; Stille, J. K.; Hegedus, L. S. *J. Am. Chem. Soc.* **1990**, *112*, 8465. (g) Ishiyama, T.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.*, **1991**, *32*, 6923. Ishiyama, T.; Miyaura, N.; Suzuki, A. *Bull. Chem. Soc. Jpn.*, **1991**, *64*, 1999. (h) Sakamoto, T.; Yasuhara, A.; Kondo, Y.; Yamanaka, H. *Chem. Pharm. Bull.* **1992**, *40*, 1137.

(3) Kondo, T.; Tsuji, Y.; Watanabe, Y. *J. Organomet. Chem.* **1988**, *345*, 397. Bumagin, N. A.; Nikitin, K. B.; Beletskaya, I. P. *Dokl. Akad. Nauk. USSR* **1991**, *320*, 619; *Chem. Abstr.* **1992**, *116*, 58663y.

(4) Ishikura, M.; Terashima, M. *Tetrahedron Lett.* **1992**, *33*, 6849 and references cited therein.

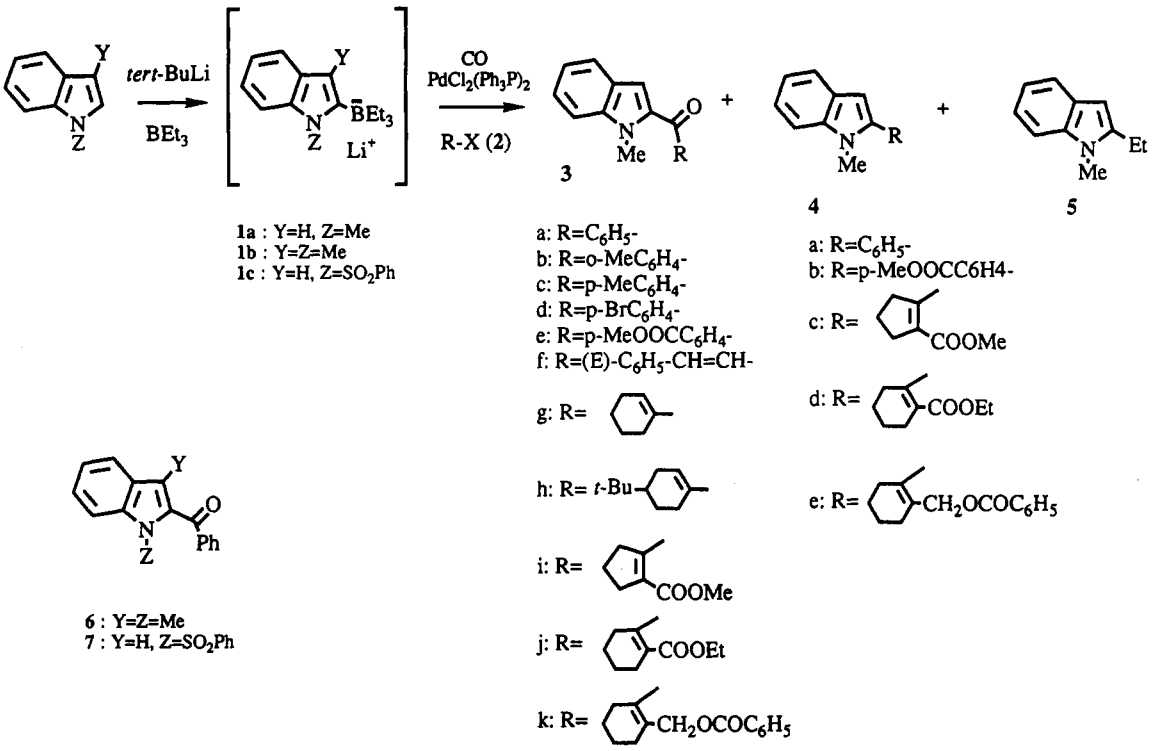
(5) Ishikura, M.; Terashima, M. *J. Chem. Soc., Chem. Commun.* **1989**, 135.

(6) Heacock, R. A.; Kasparek, S. *Adv. Heterocycl. Chem.* **1969**, *10*, 61. Remers, W. A. *The Chemistry of Heterocyclic Compounds*; Houlihan, W. J., Ed.; John Wiley & Sons, Inc.: New York, 1979; Vol. 25, Part 3, p 357. Livingstone, R. *Supplements to the 2nd edition of Rodd's Chemistry of Carbon Compounds;* Ansell, M. F., Ed.; Elsevier: Oxford, 1984; Vol. IV, Part A, p 428. Bergman, J.; Venemalm, L. *Tetrahedron* **1990**, *46*, 6061. Bergman, J.; Venemalm, L.; Gogoll, A. *Tetrahedron* **1990**, *46*, 6067.

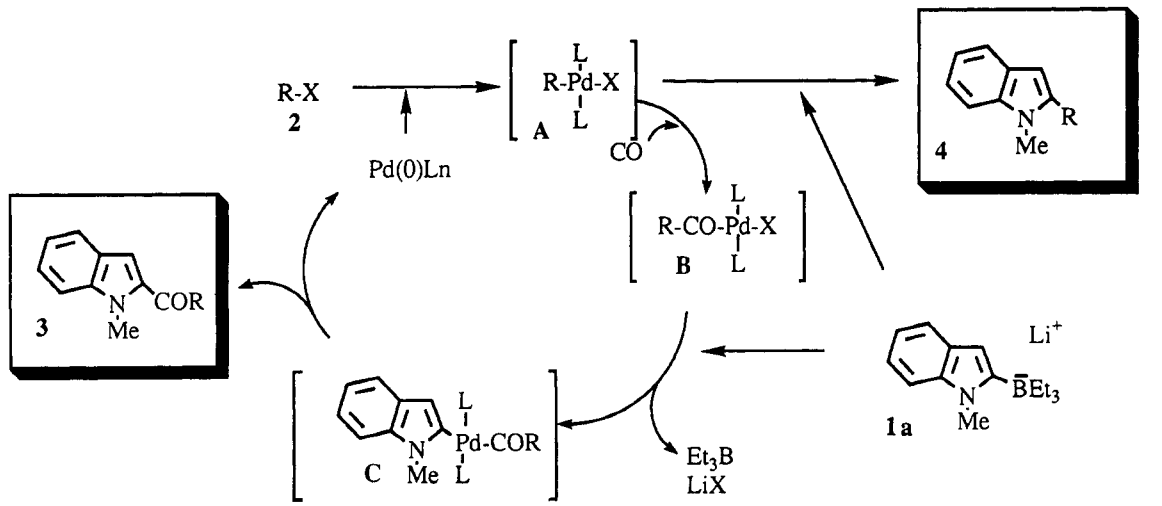
(7) (a) Garrou, P. E.; Heck, R. F. *J. Am. Chem. Soc.* **1976**, *98*, 4115. (b) Hartley, F. R. *The Chemistry of the Metal–Carbon Bond*; Patai, S., Ed.; Wiley: New York, 1985.

0022-3263/94/1959-2634$04.50/0

Scheme 1



Scheme 2



between borate **1a** and complex **A** leads to product **4**, whereas ketone **3** arises through acyl–palladium complex **B** and complex **C**. (2) The process **B** → **C** implies that increasing positive charge on the Pd of complex **B**[7a,9] may enhance the coordination–transmetalation process to form complex **C**.

Next, transformation of ketone **3** to indeno[2,1-*b*]indole was examined. Initially, cyclization of ketone **3k** with palladium catalyst [$Pd(Ph_3P)_4$, 10 mol %] in DMF at 100 °C was attempted. However, this resulted in 1,4-elimination product **8**. Heating ketone **3g** under acidic conditions afforded indole **9** as a single product,[10] in which the stereochemistry of H-6a and H-10a was assigned to be cis based on NOE experiments (the atomic numbering is shown in the structure of **9** in Chart 1). Similar acidic treatment of ketone **3h** under acidic conditions gave two isomeric products **10a** and **10b**. The all cis arrangement in **10b** was readily determined by NOE studies. A distinctive enhancement of H-6a and H-9 was observed upon irradiation of H-10a. The NOE effect between H-6a and H-10a was absent in compound **10a**.

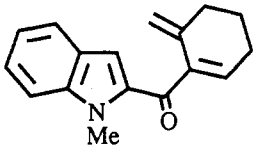
The results reported herein represent a novel application of indolylborate **1a** in the palladium-catalyzed carbonylative cross-coupling reaction to produce indol-2-yl ketone **3** in a one-pot procedure.

(8) Trost, B. M.; Verhoeven, T. R. *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: New York, 1982; Vol. 8, p 799. Milstein, D. *Acc. Chem. Res.* **1988**, *21*, 428. Stang, P. J.; Zhong, Z.; Arif, A. M. *Organometallics* **1992**, *11*, 1017.

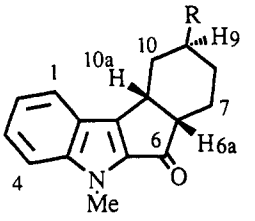
(9) Suzuki, K.; Nishida, M. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 2887. Ozawa, F.; Sugimoto, T.; Yuasa, Y.; Santra, M.; Yamamoto, T.; Yamamoto, A. *Organometallics* **1984**, *3*, 683. Huang, L.; Ozawa, F.; Yamamoto, A. *Organometallics* **1990**, *9*, 2603.

(10) Martinez, S. J.; Dalton, L.; Joule, J. A. *Tetrahedron* **1984**, *40*, 3339.

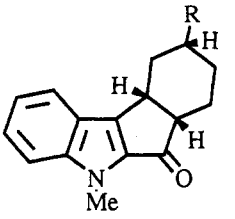
Chart 1



8



9: R=H
10a : R= *t*-Bu



10b : R=*t*-Bu

Experimental Section

General Methods. All melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. Nuclear magnetic resonance spectra were obtained in $CDCl_3$ on a JEOL EX-400 spectrometer and are reported in ppm (δ) downfield from tetramethylsilane. Infrared spectra were recorded on a Hitachi 270-30 spectrometer and are reported in wavenumbers (cm^{-1}). Mass spectra (electron inpact) are recorded at 70 eV as *m/e* and were obtained on a Shimadzu GCMS 9100-MK mass spectrometer. Tetrahydrofuran (THF) was distilled from sodium/benzophenone under a nitrogen atmosphere before use. Xylene was distilled from CaH_2 under a nitrogen atmosphere. Medium-pressure liquid chromatography (MPLC) was performed on a Merck lobar column (LiChroprep Si 60).

Phenyl 1-Methylindol-2-yl Ketone (3a): Typical Procedure. A mixture of 1-methylindole (2 mmol) and *tert*- butyllithium (1.7 M solution in pentane, 2.4 mmol) in THF (10 mL) was stirred at room temperrature for 1 h under an argon atmosphere. Triethylborane (1 M solution in hexane, 2.4 mmol) was added at −20 °C and the reaction mixture was stirred for 1 h. THF was removed *in vacuo*. Xylene (10 mL) and iodobenzene (3 mmol) were then placed in the flask, and the apparatus was filled with carbon monoxide. After the mixture was cooled to −20 °C, $PdCl_2(Ph_3P)_2$ (0.1 mmol) was added at once, and carbon monoxide was introduced up to 15 atm. The reaction mixture was gradually warmed to room temperature and heated at 90 °C for 60 h. After cooling, the mixture was treated with 10% NaOH (10 mL) and 30% H_2O_2 (2 mL) at 0 °C and diluted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$. The crude product was separated by MPLC with hexane:AcOEt (50:1) as eluent to give **3a**: bp 175 °C (0.8 Torr) [lit.[11] bp 180 °C (1 Torr)]; IR ($CHCl_3$) 1638, 1612 cm^{-1}; ^1H NMR δ 4.11 (s, 3H), 7.00 (s, 1H), 7.15 (ddd, J = 1.5, 7, 8.3 Hz, 1H), 7.30–7.50 (m, 4H), 7.56 (t, J = 7.8 Hz, 1H), 7.66 (d, J = 8.3 Hz, 1H), 7.91 (d, J = 7.5 Hz, 2H); ^{13}C NMR δ 31.8, 110.2, 114.7, 120.7, 122.8, 125.8, 128.1, 129.6, 132.0, 134.8, 139.3, 140.2, 188.3; MS 235 (M^+, base), 158; high-resolution MS calcd for $C_{16}H_{13}NO$ 235.0996, found 235.1035.

1-Methyl-2-phenylindole (4a): mp 102–103 °C (recrystallized from hexane) (lit.[12] mp 100–101 °C); ^1H NMR δ 3.75 (s, 3H), 6.51 (s, 1H), 7.14 (ddd, J = 1, 6.8, 8.3 Hz, 1H), 7.25 (ddd, J = 1, 6.8, 8.3 Hz, 1H), 7.36 (d, J = 8.3 Hz, 1H), 7.40 (d, J = 7.3 Hz, 1H), 7.45 (d, J = 7.8 Hz, 2H), 7.51 (dd, J = 7.3, 7.8 Hz, 2H), 7.63 (d, J = 8.3 Hz, 1H); ^{13}C NMR δ 31.2, 101.8, 109.7, 119.9, 120.5, 121.7, 127.9, 128.1, 128.5, 129.4, 132.9, 138.5, 141.6; MS 207 (M^+, base), 206, 178, 165.

2-Methylphenyl 1-methylindol-2-yl ketone (3b): mp 59–60 °C (recrystallized from hexane–ethyl acetate); IR ($CHCl_3$) 1638, 1614 cm^{-1}; ^1H NMR δ 2.39 (s, 3H), 4.19 (s, 3H), 6.79 (s, 1H), 7.14 (ddd, J = 1.5, 6.4, 8 Hz, 1H), 7.22–7.30 (m, 2H), 7.35–7.49 (m, 4H), 7.60 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 19.7, 32.0, 110.3, 115.8, 120.7, 123.1, 124.9, 125.7, 126.2, 128.5, 130.0, 130.8, 135.5, 136.5, 139.8, 140.5, 190.9; MS 249 (M^+, base), 232, 221, 144, 89. Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 81.94; H, 6.06; N, 5.56.

(11) Koninklijke, N. V. Belg. 637355, 1964; *Chem. Abstr.* **1965**, *62*, 7731e.

(12) Kissman, H. M.; Farnsworth, D. W.; Witkop, B. *J. Am. Chem. Soc.* **1952**, *74*, 3984.

4-Methylphenyl 1-methylindol-2-yl ketone (3c): mp 78–79 °C (recrystallized from hexane–ethyl acetate); IR ($CHCl_3$) 1632, 1612 cm^{-1}; ^1H NMR δ 2.48 (s, 3H), 4.10 (s, 3H), 6.99 (s, 1H), 7.16 (ddd, J = 1, 6.8, 7.8 Hz, 1H), 7.30 (d, J = 8 Hz, 2H), 7.39 (ddd, J = 1, 6.8, 7.8 Hz, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.84 (d, J = 8 Hz, 2H); ^{13}C NMR δ 21.6, 31.8, 110.3, 114.2, 120.6, 122.9, 125.7, 125.8, 128.8, 129.9, 135.1, 136.6, 140.1, 142.9, 188.3; MS 249 (M^+), 234 (base), 119, 89. Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 81.91; H, 6.10; N, 5.64.

4-Bromophenyl 1-methylindol-2-yl ketone (3d): mp 126–127 °C (recrystallized from hexane–ethyl acetate); IR ($CHCl_3$) 1634, 1614 cm^{-1}; ^1H NMR δ 4.12 (s, 3H), 6.99 (s, 1H), 7.17 (ddd, J = 1.5, 6, 8 Hz, 1H), 7.39–7.48 (m, 2H), 7.64 (d, J = 8.3 Hz, 2H), 7.67 (d, J = 8 Hz, 1H), 7.79 (d, J = 8.3 Hz, 2H); ^{13}C NMR δ 31.9, 110.3, 114.8, 120.9, 123.0, 125.7, 126.1, 127.1, 131.1, 131.4, 134.5, 138.1, 140.4, 187.2; MS 313 and 315 (M^+, base), 234, 158, 130, 89; high-resolution MS calcd for $C_{16}H_{12}NOBr$ 313.010 15, 315.008 13, found 313.007 11, 315.008 76. Anal. Calcd for $C_{16}H_{12}NOBr$: C, 61.67; H, 3.85; N, 4.46. Found: C, 61.49; H, 3.83; N, 4.41.

4-Carbomethoxyphenyl 1-methylindol-2-yl ketone (3e): mp 128–129 °C (recrystallized from hexane–ethyl acetate); IR ($CHCl_3$) 1722, 1638, 1614 cm^{-1} ; ^1H NMR δ 3.98 (s, 3H), 4.15 (s, 3H), 6.99 (s, 1H), 7.18 (ddd, J = 1.5, 6, 8 Hz, 1H), 7.40–7.48 (m, 2H), 7.67 (d, J = 8 Hz, 1H), 7.95 (d, J = 8.3 Hz, 2H), 8.17 (d, J = 8.3 Hz, 2H); ^{13}C NMR δ 32.0, 52.4, 110.4, 115.5, 120.9, 123.1, 125.7, 126.4, 129.4, 132.9, 134.4, 139.5, 140.5, 143.1, 166.4, 187.7; MS 293 (M^+), 234 (base), 158, 131, 89. Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.70; H, 5.15; N, 4.78. Found: C, 73.70; H, 5.11; N, 4.66.

2-(4-Carbomethoxyphenyl)-1-methylindole (4b): mp 111–112 °C (recrystallized from hexane–ethyl acetate); IR (KBr) 1712, 1608 cm^{-1}; ^1H NMR δ 3.76 (s, 3H), 3.95 (s, 3H), 6.64 (s, 1H), 7.15 (t, J = 7.8 Hz, 1H), 7.27 (t, J = 7.8 Hz, 1H), 7.37 (d, J = 7.8 Hz, 1H), 7.58 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 7.8 Hz, 1H), 8.13 (d, J = 8.3 Hz, 2H); ^{13}C NMR δ 31.3, 52.1, 102.8, 109.7, 120.1, 120.7, 122.3, 127.8, 128.9, 129.2, 137.3, 128.8, 140.2, 166.7; MS 265 (M^+, base), 264, 234, 205, 102. Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.01; H, 5.63; N, 5.27.

(*E*)-Cinnamyl 1-methylindol-2-yl ketone (3f): mp 87–88 °C (recrystallized from hexane–ethyl acetate); IR ($CHCl_3$) 1648, 1612 cm^{-1}; ^1H NMR δ 4.14 (s, 3H), 7.14–7.22 (m, 1H), 7.38–7.48 (m, 6H), 7.55 (d, J = 16 Hz, 1H), 7.63–7.70 (m, 2H), 7.72 (d, J = 7.8 Hz, 1H), 7.81 (d, J = 16 Hz, 1H); ^{13}C NMR δ 32.1, 110.3, 111.5, 120.7, 122.9, 123.9, 123.7, 125.9, 128.3, 128.8, 130.2, 134.90, 136.1, 140.4, 142.5, 182.5; MS 261(M^+, base), 232, 184, 170, 144. Anal. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.86; H, 5.70; N, 5.23.

Cyclohexen-1-yl 1-methylindol-2-yl ketone (3g): IR (neat) 1716, 1624 cm^{-1}; ^1H NMR δ 1.65–1.85 (m, 4H), 2.30 (brs, 2H), 2.45 (brs, 2H), 3.96 (s, 3H), 6.83–6.87 (m, 1H), 6.95 (s, 1H), 7.14 (ddd, J = 1.5, 6.3, 8 Hz, 1H), 7.32–7.40 (m, 2H), 7.68 (d, J = 8 Hz, 1H); ^{13}C NMR δ 21.7, 22.1, 24.1, 26.0, 31.5, 110.1, 112.0, 120.3, 122.5, 125.0, 125.8, 135.3, 140.0, 141.8, 189.9; MS 239 (M^+), 210, 182, 158, 89 (base); high-resolution MS calcd for $C_{16}H_{17}NO$ 239.1309, found 239.1251.

4-*tert*-Butylcyclohexen-1-yl 1-methylindol-2-yl ketone (3h): IR (neat) 1668, 1628 cm^{-1}; ^1H NMR δ 0.93 (s, 9H), 1.15–1.30 (m, 1H), 1.35–1.45 (m, 1H), 1.95–2.35 (m, 2H), 2.25–2.45 (m, 2H), 2.65–2.75 (m, 1H), 3.96 (s, 3H), 6.84–6.90 (m, 1H), 6.96 (s,

1H), 7.14 (t, J = 7.8 Hz, 1H), 7.32–7.42 (m, 2H), 7.66 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 23.5, 27.0, 27.1, 27.8, 31.5, 32.2, 43.5, 110.1, 112.0, 120.4, 122.5, 125.0, 125.8, 135.4, 139.9, 142.3, 189.7; MS 295 (M^+, base), 210, 158, 107, 89; high-resolution MS calcd for $C_{20}H_{25}NO$ 295.1934, found 295.1940.

2-Carbomethoxycyclopenten-1-yl 1-methylindol-2-yl ketone (3i): mp 116–117 °C (recrystallized from hexane–ethyl acetate); IR ($CHCl_3$) 1712, 1632, 1614 cm^{-1}; ^{1}H NMR δ 2.08–2.18 (m, 2H), 2.80–2.89 (m, 2H), 2.90–2.97 (m, 2H), 3.51 (s, 3H), 4.15 (s, 3H), 7.03 (s, 1H), 7.14 (ddd, J = 2, 5.5, 8 Hz, 1H), 7.36–7.44 (m, 2H), 7.65 (d, J = 8 Hz, 1H); ^{13}C NMR δ 22.6, 32.0, 33.2, 38.0, 51.5, 110.3, 113.2, 120.7, 122.9, 125.9, 126.1, 133.7, 134.2, 140.5, 153.8, 164.6, 188.9; MS 283 (M^+), 224 (base), 196, 158, 130. Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.06; H, 6.05; N, 4.94. Found: C, 72.05; H, 6.10; N, 4.86.

2-(2-Carbomethoxycyclopenten-1-yl)-1-methylindole (4c): IR (neat) 1704, 1635 cm^{-1}; ^{1}H NMR δ 2.00–2.10 (m, 2H), 2.80–2.90 (m, 4H), 3.57 (s, 3H), 3.59 (s, 3H), 6.44 (s, 1H), 7.08 (t, J = 7.8 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 7.25 (d, J = 7.8 Hz, 1H), 7.60 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 22.0, 30.7, 34.6, 40.9, 51.3, 101.1, 109.4, 119.5, 120.5, 121.7, 127.6, 132.6, 136.2, 137.8, 144.9, 165.4; MS 255 (M^+), 224, 196 (base), 180, 167; high-resolution MS calcd for $C_{16}H_{17}NO_2$ 255.1258, found 255.1245.

2-Carbethoxycyclohexen-1-yl 1-methylindol-2-yl ketone (3j): IR (neat) 1710, 1644, 1614 cm^{-1}; ^{1}H NMR δ 0.95 (t, J = 7.3 Hz, 3H), 1.75–1.90 (m, 4H), 2.40–2.60 (m, 4H), 3.91 (q, J = 7.3 Hz, 2H), 4.15 (s, 3H), 6.97 (s, 1H), 7.12 (ddd, J = 1.5, 6.3, 7.8 Hz, 1H), 7.30–7.50 (m, 2H), 7.63 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 13.7, 21.5, 21.7, 24.9, 29.4, 31.9, 60.6, 110.2, 112.2, 120.6, 122.9, 125.7, 128.4, 134.2, 140.3, 149.3, 166.5, 192.1; MS 311 (M^+), 265, 238, 181, 153 (base); high-resolution MS calcd for $C_{19}H_{21}NO_3$ 311.1520, found 311.1510.

2-(2-Carbethoxycyclohexen-1-yl)-1-methylindole (4d): IR (neat) 1700 cm^{-1}; ^{1}H NMR δ 0.67 (t, J = 7.3 Hz, 3H), 1.75–1.85 (m, 4H), 2.39 (brs, 2H), 2.50 (brs, 2H), 3.57 (s, 3H), 3.82 (q, J = 7.3 Hz, 2H), 6.23 (s, 1H), 7.06 (t, J = 6.8 Hz, 1H), 7.16 (t, J = 6.8 Hz, 1H), 7.26 (d, J = 7.8 Hz, 1H), 7.53 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 13.5, 21.9, 22.3, 26.4, 30.2, 33.1, 60.2, 99.1, 109.1, 119.3, 120.3, 121.1, 127.9, 133.1, 137.1, 137.2, 141.6, 168.7; MS 283 (M^+, base), 238, 210, 181, 168, 153; high-resolution MS calcd for $C_{18}H_{21}NO_2$ 283.1571, found 283.1582.

2-(Benzoxymethyl)cyclohexen-1-yl 1-methylindol-2-yl ketone (3k): IR (neat) 1716, 1638, 1614 cm^{-1}; ^{1}H NMR δ 1.79 (brs, 4H), 2.29 (brs, 2H), 2.41 (brs, 2H), 4.03 (s, 3H), 4.74 (s, 2H), 7.10 (ddd, J = 1.5, 6.4, 8.3 Hz, 1H), 7.19 (s, 1H), 7.25–7.40 (m, 4H), 7.47 (t, J = 7.3 Hz, 1H), 7.59 (d, J = 8 Hz, 1H), 7.86 (d, J = 8.3 Hz, 2H); ^{13}C NMR δ 22.0, 22.1, 26.7, 28.4, 31.9, 65.3, 110.3, 114.7, 120.7, 123.0, 125.8, 126.1, 128.1, 129.4, 129.8, 131.7, 132.8, 134.3, 138.2, 140.6, 166.1, 192.6; MS 373 (M^+), 252 (base), 105; high-resolution MS calcd for $C_{24}H_{23}NO_3$ 373.1676, found 373.1659.

2-(2-(Benzoxymethyl)cyclohexen-1-yl)-1-methylindole (4e): IR (neat) 1718 cm^{-1}; ^{1}H NMR δ 1.80 (brs, 4H), 2.31 (brs, 4H), 3.61 (s, 3H), 4.68 (s, 2H), 6.30 (s, 1H), 7.08 (t, J = 7.4 Hz, 1H), 7.18 (t, J = 7.4 Hz, 1H), 7.28 (d, J = 7.3 Hz, 1H), 7.38–7.42 (m, 2H), 7.50–7.60 (m, 2H), 7.99 (d, J = 8 Hz, 2H); ^{13}C NMR δ 22.4, 22.7, 26.9, 30.1, 32.1, 66.2, 100.4, 109.3, 119.5, 120.3, 121.1, 127.9, 128.4, 129.7, 129.8, 130.3, 132.9, 134.7, 137.3, 1490.4, 166.2; MS 345 (M^+), 240 (base); high-resolution MS calcd for $C_{23}H_{23}NO_2$ 345.1706, found 345.1727.

Phenyl 1,3-dimethylindol-2-yl ketone (6): mp 56–58 °C (recrystallized from hexane) (lit.[13] mp 55–56 °C); IR ($CHCl_3$) 1632 cm^{-1}; ^{1}H NMR δ 2.11 (s, 3H), 3.84 (s, 3H), 7.16 (ddd, J = 2, 6, 8 Hz, 1H), 7.35–7.42 (m, 2H), 7.46–7.52 (m, 2H), 7.59 (tt, J = 1.5, 7.3 Hz, 1H), 7.63 (d, J = 8 Hz, 1H), 7.85 (dd, J = 1.5, 8.3 Hz, 2H); ^{13}C NMR δ 11.0, 31.6, 110.0, 118.6, 119.8, 120.7, 125.4, 127.5, 128.5, 129.7, 132.7, 133.7, 138.9, 139.9, 190.2; MS 249 (M^+), 248, 172, 66, 69(base).

1-(Phenylsulfonyl)indol-2-yl ketone 7: mp 141–142 °C (recrystallized from hexane-ethyl acetate) (lit.[14] mp 142–143 °C); IR ($CHCl_3$) 1662, 1660 cm^{-1}; ^{1}H NMR δ 6.95 (s, 1H), 7.30 (dt, J = 1, 7.8 Hz, 1H), 7.44–7.52 (m, 5H), 7.57 (d, J = 7.8 Hz, 2H), 7.59–7.65 (m, 1H), 7.98 (dd, J = 1.5, 8Hz, 2H), 8.08 (dd, J = 1.5, 8 Hz, 2H), 8.15(dd, J = 1, 8Hz, 1H); ^{13}C NMR δ 115.1, 116.9, 122.6, 124.3, 127.5, 128.5, 128.6, 128.9, 129.9, 133.5, 133.9, 137.4, 137.7, 137.9, 138.2, 187.5; MS 361 (M^+), 220 (base), 165, 105.

5,6,6a,7,8,9,10,10a-Octahydro-5-methylindeno[2,1-b]indole (9): A solution of ketone **3g** (300 mg) and 10% HCl (3 mL) in dioxane (5 mL) was heated at 100 °C for 6 h. The mixture was concentrated and diluted with ethyl acetate (60 mL). The organic layer was washed with saturated sodium bicarbonate several times and brine and dried over $MgSO_4$. After the solvent was removed, the residue was separated by MPLC with hexane–ethyl acetate (20:1) as eluent to give 210 mg (70%) of **9**: mp 84–85 °C (recrystallized from hexane–ethyl acetate); IR ($CHCl_3$) 1676 cm^{-1}; ^{1}H NMR δ 1.35–1.65 (m, 5H), 1.80–1.95 (m, 1H), 1.95–2.05 (m, 1H), 2.15–2.30 (m, 1H), 3.00–3.10 (m, 1H), 3.49–3.55 (m, 1H), 3.92 (s, 3H), 7.16 (ddd, J = 1.5, 6.4, 8.3 Hz, 1H), 7.35–7.43 (m, 2H), 7.70 (d, J = 8.3 Hz, 1H); ^{13}C NMR δ 20.7, 20.8, 23.3, 28.4, 30.1, 33.4, 52.5, 110.9, 120.0, 121.8, 122.7, 126.4, 137.9, 144.6, 147.6, 197.2; MS 239 (M^+), 211, 197, 194 (base), 181, 169. Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.26; H, 6.99; N, 5.90.

5,6,6a,7,8,9,10,10a-Octahydro-9-*tert*-butyl-5-methylindeno-[2,1-*b*]indole (10). By use of the procedure described above, **10a** (60%) and **10b** (11%) were isolated by MPLC (hexane–ethyl acetate (20:1) as eluent) from ketone **3h**. **10a**: IR (neat) 1686 cm^{-1}; ^{1}H NMR δ 0.76 (s, 9H), 0.95–1.05 (m, 1H, H-9), 1.20–1.30 (m, 1H), 1.40–1.50 (m, 1H), 1.70–1.80 (m, 1H), 1.85–1.95 (m, 2H), 2.17 (dt, J = 13.7, 3.4 Hz, 1H), 3.01 (q, J = 4.4 Hz, 1H, H-6a), 3.72–3.77 (m, 1H, H-10a), 3.92 (s, 3H), 7.15 (ddd, J = 1.5, 6.4, 7.8 Hz, 1H), 7.35–7.43 (m, 2H), 7.71 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 21.7, 24.1, 26.1, 26.9, 30.1, 32.9, 33.4, 39.2, 52.2, 111.0, 120.1, 121.7, 123.0, 126.4, 138.8, 144.9, 147.0, 198.1; MS 295 (M^+, base), 210, 196, 170, 144; high-resolution MS calcd for $C_{20}H_{25}NO$ 295.1936, found 295.1917.

10b: IR (neat) 1686 cm^{-1}; ^{1}H NMR δ 0.84 (s, 9H), 0.95 (q, J = 12.7 Hz, 1H), 1.20–1.30 (m, 1H), 1.33–1.43 (m, 1H), 1.60–1.70 (m, 1H, H-9), 1.85–1.95 (m, 2H), 2.29–2.38 (m, 1H), 2.98 (dd, J = 7.5, 13 Hz, 1H, H-6a), 3.42 (dt, J = 12.2, 5.8 Hz, 1H, H-10a), 3.90 (s, 3H), 7.17 (ddd, J = 1.5, 6.9, 7.8 Hz, 1H), 7.34–7.43 (m, 2H), 7.73 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 23.7, 23.9, 27.1, 30.0, 31.0, 32.9, 34.9, 44.7, 52.4, 110.9, 120.0, 121.9, 122.5, 126.4, 137.3, 144.6, 148.0, 196.8; MS 295 (M^+, base), 210, 196, 168, 144; high-resolution MS calcd for $C_{20}H_{25}NO$ 295.1936, found 295.1954.

Supplementary Material Available: ^{1}H NMR spectra for compounds **3g**, **3h**, **3j**, **3k**, and **4c–e** and 1DIFNOE spectra for **10a** and **10b** (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(13) Shvedov, V. I.; Alekseev, V. V.; Grinev, A. N. *Khim. Farm. Zh.* **1968**, *2*, 8; *Chem. Abstr.* **1969**, *70*, 11469f.
(14) Sundberg, R. J.; Russell, H. F. *J. Org. Chem.* **1973**, *38*, 3324.